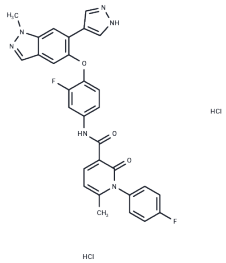
Data Sheet (Cat.No.T15808)

TargetMol

Merestinib dihydrochloride

Chemical Properties



CAS No. : 1206801-37-7

Formula: C30H24Cl2F2N6O3

Molecular Weight: 625.45

Storage: Keep away from moisture,Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Merestinib dihydrochloride (LY2801653 dihydrochloride) is an orally available kinase inhibitor with antitumor activity that inhibits MET, AXL, RON, and MKNK1/2, and inhibits the growth of NTRK fusion-carrying tumors.
Targets(IC50)	Discoidin Domain Receptor (DDR),FLT,c-Met/HGFR,ROS Kinase,TAM Receptor,Tyrosine Kinases
In vitro	Merestinib dihydrochloride is a potent, orally bioavailable c-Met inhibitor with a Ki value of 2 nM and significant antitumor activity. In addition, Merestinib dihydrochloride showed significant antitumor activity against MST1R (IC50=11 nM), FLT3 (IC50=7 nM), AXL (IC50=2 nM), MERTK (IC50=10 nM), TEK (IC50=63 nM), ROS1, DDR1/2 (IC50=0.1/7 nM) and MKNK1/2 (IC50=7 nM) showed potent activity. Merestinib dihydrochloride affected MET pathway-dependent cell scattering and proliferation. In HGF-stimulated H460 cells, the mean IC50 value for Merestinib dihydrochloride on MET autophosphorylation was 35.2 nM, compared to 59.2 nM in S114 cells. Transfection of MET variants gave cells growth factor independence, and treatment with Merestinib dihydrochloride was able to inhibit the growth of these MET variant clones with IC50 values ranging from approximately 3-fold more potent (V1092I) to approximately 6-fold less potent (L1195V) compared to MET wild-type sequences. [1] [2]
In vivo	Merestinib dihydrochloride showed significant antitumor effects in a MET-amplified xenograft model (MKN45), a MET autocrine model (U-87MG and KP4), and a MET overexpression model (H441), as well as in vivo vasculature normalization. As a type II ATP-competitive inhibitor, Merestinib dihydrochloride is a slow dissociating inhibitor of MET tyrosine kinase with a pharmacodynamic residence time (Koff) of 0.00132 min^-1 and a half-life (t1/2) of 525 min.Merestinib dihydrochloride treatment inhibited MET phosphorylation with a combined TED50 (50% targeted inhibitor dose) of 1.2 mg/kg and TED90 (90% targeted inhibitor dose) of 7.4 mg/kg.With Merestinib dihydrochloride (20 mg/kg), TFK-1 tumor growth was significantly lower than that of the control group. In addition, Merestinib dihydrochloride effectively inhibited the growth of intrahepatic and extrahepatic cholangiocarcinoma (CCC) xenograft tumors. [1][2]

Solubility Information

Solubility	DMSO: 80 mg/mL (127.91 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (5.28 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.5988 mL	7.9942 mL	15.9885 mL
5 mM	0.3198 mL	1.5988 mL	3.1977 mL
10 mM	0.1599 mL	0.7994 mL	1.5988 mL
50 mM	0.032 mL	0.1599 mL	0.3198 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Yan SB, et al. LY2801653 is an orally bioavailable multi-kinase inhibitor with potent activity against MET, MST1R, and other oncoproteins, and displays anti-tumor activities in mouse xenograft models. Invest New Drugs. 2013 Aug;31(4):833-44.

Barat S, et al. Targeting c-MET by LY2801653 for treatment of cholangiocarcinoma. Mol Carcinog. 2016 Dec;55(12): 2037-2050.